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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/783,669	02/14/2001	D. Wade Walke	LEX-0135-USA	9659

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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/04/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/783,669	WALKE ET AL	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Claims 1-4 have been amended and claims 5-7 have been added as requested in the amendment of Paper No. 11, filed on September 04, 2002. Claims 1-7 are pending in the instant application.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on September 04, 2002 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

5. Claims 1-7 stand rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record as applied to claims 1-4 in section 3 of Paper No. 7. Briefly, the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

Applicant submits that one of the examples of utility of the present invention is that "the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins" (page 7, last paragraph of the Response), as well as credible and well-established utility is supported by the information "that more than half of the currently marketed

drugs target proteins that are structurally (7TM proteins) and functionally (G-protein interaction) related to the presently described sequences" (page 4, second paragraph). Applicant further argues that reference of Ji et al. (incorrectly identified as Tae et al. in the previous office action), in fact, supports "that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of [particular subfamily of GPCR proteins]" (page 3, second paragraph). Additionally, Applicant submits that reference of Skolnick et al. admits that "sequence-based approaches to protein-function prediction have proved to be very useful", and that publication of Yan et al. cites only one example when two amino acid change in ligand structure lead to binding to two distinct receptors. Applicant's arguments have not been found persuasive for the following reasons.

Applicant asserts that a protein of the instant invention belongs to a family of proteins of which some members are the targets of over 50% of the therapeutic agents currently on the market. This number is actually higher since a number of agents such as antidepressants and hypertension medications were being employed clinically before their site of action was known. However, each clinical agent, which has been developed by measuring its interaction with a specific G protein-coupled receptor, was evaluated against a receptor whose native ligand and physiological function were known, such as the adrenergic receptors, the dopamine receptors and the serotonin receptors. There are also numerous G protein-coupled receptors, which do not mediate clinically significant process. More importantly, an artisan knew, before they employed a specific G protein-coupled receptor to identify clinically useful compounds, which physiological process or processes they wished to manipulate and that the protein employed in their assay had an influence of that process. Even if one identifies an agonist or antagonist for a

receptor of the instant invention, this information is useless since one has no idea of what clinical effect the administration of that agonist or antagonist to an individual would have.

The fact that the sequences of the instant invention "can be used to track the expression of the genes encoding the described proteins" cannot serve as a basis for a specific utility of the claimed sequences for the obvious reason. Any human protein is eventually encoded by a specific locus, and, although isolation of a novel sequence can undoubtedly be recognized as a scientific achievement, without knowledge of specific biological significance of the instant nucleic acid molecule or the proteins encoded thereby there is not immediate use for the claimed sequences. Applicant asserts the biological function of the claimed novel GPCRs based on structural similarities and homology to the known GPCR. The references quoted in the previous office action of Paper No. 7 all support the general idea that structural similarity does not necessarily lead to certain functional predictions. Persons skilled in the art know that changing one amino acid in a sequence gives, by definition, a new protein. Therefore, one cannot assume *a priori* that such change will not significantly alter the properties of a protein (see Introduction to proteins and protein Engineering, 1986, Elsevier, p.41). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes)" (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

Applicant refers to *Juicy Whip v. Orange Bang* (Fed. Cir. 1999), which held that in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful

result", and to *Cross v. Iizuka* (Fed. Cir. 1985), which stated that "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101" (page 5, second paragraph). Applicant further presents "[a]s just one example of utility of the present nucleotide sequences, [...] [that they] can be used to track the expression of the genes encoding the described proteins" (page 5, last paragraph) . This has not been found to be persuasive. The employment of polynucleotides of the instant invention, or a nucleic acid encoding that protein, "to track the expression of the genes encoding the described proteins " or, in other words, as a tissue specific marker is not a substantial or specific utility. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein, which is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein, which is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

One could just as readily argue that any purified compound having a known structure could be employed as an analytical standard in such processes as nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and mass spectroscopy as well as in polyacrylamide gel electrophoresis (PAGE), high performance liquid chromatography (HPLC) and gas chromatography. None of these processes could be practiced without either calibration standards having known molecular structures or, at least, a range of molecular weight markers having known molecular weights. One could further extrapolate upon this premise by asserting that any item having a fixed measurable parameter can be employed to calibrate any machine or process which measures that parameter. For example, any item having a constant mass within an acceptable range can be employed to calibrate a produce scale in a grocery store. The calibration of produce scales is certainly an important function since most states require produce scales to be calibrated and certified. Therefore, to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound, which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a hydrocarbon it certainly could have been employed in the well-known process of combustion for purposes of lighting and/ or the generation of heat. The generation of heat by combustion of hydrocarbons certainly

was and remains an important process. Irrespective of such obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility.

To grant Applicant a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed polynucleotide based solely upon an assertion that the protein encoded thereby can be employed as a tissue marker is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a fuel source.

Applicant's reliance on *In re Brana*, 51 F.3d 1560,1566, 34 USPQ2d 1436,1441 (Fed. Cir. 1995) is misplaced (page 6 of the Response). That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established specific and substantial utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive *in vitro* data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. The protein of the instant invention does not belong to a family of compounds with a common well-established specific and substantial utility. The

utility of those members of the receptor family to which the claimed protein in the instant application belongs lies in the knowledge that they modulate a specific physiological activity in response to a specific ligand. Since the instant specification does not disclose the identity of a native ligand for the claimed protein, knowledge of the pathway through which that receptor transduces its signal in response to that ligand is not particularly useful.

Finally, Applicant submits that the polynucleotides of the instant invention have substantial, credible and well-established utility because "the claimed polynucleotide sequences define how the encoded exons are actually splices together to produce an active transport" (page 8, last paragraph), and that "persons skilled in the art [...] readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically, human genomic data" (page 9, second paragraph). The Examiner agrees that there is little doubt that after complete characterization the claimed nucleic acid and encoded proteins may be found to have a specific and substantial credible utility. However, this characterization is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. To employ a polynucleotide of the instant invention as the object of further research has been determined by the courts to be a utility, which, alone, does not support patentability.

Applicant's arguments that the office has issued other GPCR patents (page 10, last paragraph) are not persuasive. It is well settled that the prosecution of one patent application does not affect the prosecution of an unrelated application. *In re Wertheim*, 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976) (holding that "[I]t is immaterial in *ex parte* prosecution whether the same or similar claims have been allowed to others"). Accordingly, Applicant's arguments with respect to the issued U.S. Patent 6,043,052 are unavailing.

Claim Rejections - 35 USC § 112

6. Claims 1-7 stand rejected under 35 U.S.C. 112, first paragraph for reasons of record as applied to claims 1-4 in section 4 of Paper No. 7. Briefly, because the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
December 3, 2002

JOHN ULM
PRIMARY EXAMINER
GROUP 1600